# Impaired Cortisol Homeostasis in Patients with Obstructive Sleep Apnea

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## Abstract

**Introduction:** Obstructive sleep apnea (OSA) may affect cortisol metabolism. The aim of this study was to investigate potential changes in cortisol levels in patients with OSA according to disease severity by combining plasma cortisol measurements with cumulative urinary cortisol assessment. We hypothesized that nocturnal urinary cortisol levels would be higher in patients with severe OSA than in those with moderate OSA.

**Methods:** The study included 58 male patients referred to the Sleep Medicine Centre of University Clinical Hospital Mostar because of an increased risk of OSA. Disease severity was determined using overnight polysomnography (PSG) and the apnea–hypopnea index (AHI). Patients were divided into two groups: moderate OSA (AHI 15–<30) and severe OSA (AHI ≥30). The groups were compared according to morning plasma cortisol concentrations and 24-hour cumulative urinary cortisol, with urine samples divided into daytime and nighttime collections. Correlations between AHI and morning plasma cortisol concentrations, as well as cumulative urinary cortisol levels, were also examined. Multiple linear regression analysis adjusted for age and body mass index (BMI) was used to assess independent associations with AHI.

**Results:** No statistically significant differences were observed between patients with severe and moderate OSA in morning plasma cortisol concentrations ($p$ = 0.188) or daytime urinary cortisol levels ($p$ = 0.153). However, nocturnal urinary cortisol levels were significantly higher in patients with severe OSA (69.3 ± 58.3 vs. 45.9 ± 23.2 mmol/L; $p$ = 0.042), as were 24-hour urinary cortisol levels (143.1 ± 75.2 vs. 102.6 ± 38.8 mmol/L; $p$ = 0.011). In the overall study population (n = 58), AHI showed a significant positive correlation with nocturnal urinary cortisol levels ($r$ = 0.287; $p$ = 0.014). Furthermore, in a multiple linear regression model adjusted for age and BMI, nocturnal urinary cortisol levels remained significantly associated with AHI (β ± SE = 0.679 ± 0.31; $p$ = 0.028).

**Conclusion:** Patients with severe OSA had significantly higher nocturnal urinary cortisol levels than patients with moderate OSA. These findings provide additional evidence of an association between OSA and increased nocturnal cortisol secretion and suggest that cumulative urinary cortisol measurements may have clinical utility.

**Keywords:** obstructive sleep apnea; OSA severity; cortisol; urinary cortisol



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# Poremećaj homeostaze kortizola u bolesnika s opstruktivnom apnejom u spavanju

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## Sažetak

**Uvod:** Opstruktivna apneja u spavanju (OSA) može utjecati na metabolizam kortizola. Cilj ovog istraživanja bio je ispitati moguće promjene razina kortizola u bolesnika s OSA-om ovisno o težini bolesti, kombiniranjem mjerenja kortizola u plazmi i procjene kumulativnog izlučivanja kortizola urinom. Pretpostavljeno je da će razine kortizola u noćnom urinu biti više u bolesnika s teškom OSA-om nego u bolesnika s umjerenom OSA-om.

**Metode:** Istraživanje je obuhvatilo 58 muških bolesnika upućenih u Centar za medicinu spavanja Sveučilišne kliničke bolnice Mostar zbog povećanog rizika za OSA-u. Težina bolesti određena je cjelonoćnom polisomnografijom (PSG) i indeksom apneje i hipopneje (AHI). Bolesnici su podijeljeni u dvije skupine: s umjerenom OSA-om (AHI 15–<30) i teškom OSA-om (AHI ≥30). Skupine su uspoređene prema koncentracijama jutarnjeg kortizola u plazmi i 24-satnom kumulativnom izlučivanju kortizola urinom, pri čemu su uzorci urina bili podijeljeni na dnevnu i noćnu porciju. Ispitane su i korelacije između AHI-ja i jutarnjih koncentracija kortizola u plazmi te kumulativnih razina kortizola u urinu. Za procjenu neovisnih povezanosti s AHI-jem primijenjena je višestruka linearna regresijska analiza prilagođena dobi i indeksu tjelesne mase (ITM).

**Rezultati:** Nisu utvrđene statistički značajne razlike između bolesnika s teškom i umjerenom OSA-om u koncentracijama jutarnjeg kortizola u plazmi ($p$ = 0,188) ni u razinama kortizola u dnevnom urinu ($p$ = 0,153). Međutim, razine kortizola u noćnom urinu bile su značajno više u bolesnika s teškom OSA-om (69,3 ± 58,3 prema 45,9 ± 23,2 mmol/L; $p$ = 0,042), kao i razine kortizola u 24-satnom urinu (143,1 ± 75,2 prema 102,6 ± 38,8 mmol/L; $p$ = 0,011). U ukupnoj skupini ispitanika (n = 58) AHI je pokazao značajnu pozitivnu korelaciju s razinama kortizola u noćnom urinu ($r$ = 0,287; $p$ = 0,014). Nadalje, u modelu višestruke linearne regresije prilagođenom dobi i ITM-u, razine kortizola u noćnom urinu ostale su značajno povezane s AHI-jem (β ± SE = 0,679 ± 0,31; $p$ = 0,028).

**Zaključak:** Bolesnici s teškom OSA-om imali su značajno više razine kortizola u noćnom urinu u usporedbi s bolesnicima s umjerenom OSA-om. Ovi nalazi pružaju dodatne dokaze o povezanosti OSA-e s povećanim noćnim izlučivanjem kortizola i upućuju na moguću kliničku korisnost kumulativnog mjerenja kortizola u urinu.

**Ključne riječi:** opstruktivna apneja u spavanju; težina OSA-e; kortizol; kortizol u urinu



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